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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

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EXAMINER

ART UNIT	PAPER NUMBER

DATE MAILED: [illegible]

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

DETAILED ACTION

1. This action is in response to the papers filed January 30, 2002. Currently, claims 1-10, 12 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

3. This action contains new grounds of rejection necessitated by amendment

4. The examiner notes that the clean copy of the claims provided on page 2 of the response and the marked up copy of the claims, on page 13, are different. The preamble of the clean copy is for detecting, the preamble for the marked up copy is for detecting or quantitating. In order to facilitate compact prosecution, the examiner has addressed both preambles.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-10, 12 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Methods for detecting or quantitating oligonucleotides by contacting sample with probes, capturing the probes degrading single stranded probes and detecting labels lacks steps critical or essential to the practice of the invention. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The claimed method has been limited to a method consisting of detecting (or quantitating) an oligonucleotide in a bodily fluid or extract by contacting said fluid with a probe complementary to said oligonucleotide to form double stranded complexes, capturing the binding moieties on a solid support, contacting the oligonucleotides with a nuclease and detecting.

The specification, teaches that the "cutting assay" is summarized in Figures 1 and 2. As shown in Figure 1, a schematic diagram showing the mechanism of the nuclease-based cutting assay of the present invention (page 4). Figure 2 illustrates the assay method. Figure 2 illustrates two wash steps, prior to and following the nuclease reaction in addition to following antibody detection.

The method, as set out in the claims, appears to be missing essential steps which are critical to the enablement of the method. First, the method as claimed does not contain any wash steps. Once the hybrid (analyte and template probes) molecules are bound to the plate, Figure 2 illustrates that a wash step is required. The wash step will remove any of the unbound sample and other material which will cause background and inhibit detection. The instant specification does not provide how to perform the method absent a wash step following capture on the solid support. A wash step following the nuclease reaction is also an essential step. In the event that a wash step did not follow the nuclease reaction, label which was previously attached to the solid support would be in the solution and detectable. Without removal of this label in the solution, detection would be present in all assays. Thus, this wash step appears also to

be essential to the method described in the specification. Similarly, incubation, and stop solutions appear to be essential steps in Example 1 (pages 23-25).

Secondly, the claim broadly encompasses detection of an oligonucleotide in a bodily fluid or extract. Since bodily fluid or extracts encompass untreated samples, no preparation is permitted in the instant method. The specification teaches that the bodily fluid and/or extract may be prepared or may be selected from tissue, bond or organ samples, serum, feces and blood cells (page 22). The instant method has not provided enablement for merely contacting whole blood, bones or feces, for example, with a probe and obtaining accurate results. The method would require preparatory steps prior to the contacting fluid step which has not been permitted in the instant method. However, in the event that the claims are intended to encompass any sample processing necessary, the treating of the sample with a base to render the target nucleic acid accessible to hybridization and if necessary, nicking the sample, as taught by Impraim, would also be permissible. Thus, the scope of the method has not been enabled.

Finally, as written the claim does not provide that it is possible that the oligonucleotide of interest (target) is not present in the sample. The claim requires that hybrids and single stranded oligonucleotides are formed. Thus, the claim will not work in the event that the sample is not present.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-10, 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-10, 12 are indefinite because the claims do not recite a positive process step which clearly relates back to the preamble. The preamble states that the method is for detecting or quantitating but the final process step is detecting. Therefore the claims are unclear as to whether the method is a method of detecting and quantitating or merely a method of detecting.

Response to Arguments

The response asserts, on page 3 of the response filed January 30, 2002, that "applicants have amended the claims to recite a quantitating step in the process". This argument has been reviewed but is not convincing because marked up copy Claim 1 does not have a quantitating step. The clean version of the claims, makes no mention of quantitating either in the preamble or in the final process step. With respect to the clean claims, page 2 of the response, the claim is directed to a method of detecting an oligonucleotide, whereas the final step detects a label which is indicative of a double stranded oligonucleotide moieties bound to said solid support. Thus, the claim is not clear whether the oligonucleotides are detected or rather double-stranded oligonucleotide moieties bound to said solid supports are detected. Thus for the reasons above and those already of record, the rejection is maintained.

B1) Claim 12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 is limited to a method consisting of steps (a)-(d). Claim 1 is not permissive of any additional steps. Therefore, Claim 12 which proposes an additional step is improper. Furthermore, in the event that applicant were to rewrite Claim 1 containing steps (a)-(d) and further comprising (e), the claim would indefinite because it is unclear whether the method only adds a single step or whether the method is now permissive of any additional steps, i.e. a comprising method such that the art previously presented would be appropriate (namely Impraim et al.).

C1) Claims 1-10, 12 are indefinite over the recitation "single-stranded and double-stranded oligonucleotide moieties are formed". It is unclear what a double stranded oligonucleotide moiety is. The probes comprise a marker and a binding moiety. It is unclear how these moieties are related. The "single-stranded and double-stranded oligonucleotide moieties" may be appropriately described as hybrids between the target of interest and the probe. However, as written, the elements of the claim are unclear.

D1) Claims 1-10, 12 are directed to detecting an oligonucleotide, however, the claim appears to require that the oligonucleotide is present since the claim requires in step a that double stranded moieties are formed. Therefore, the claim will not work when there is no oligonucleotide (target) present in the fluid or extract.

E1) Claims 1-10, 12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are washing steps. Claims 1-10, 12 are directed to detecting the presence of a label as indicative of double-stranded oligonucleotide moieties, however, since the claim does not contain a wash step or a removing step to remove all of the "probes which comprise a detectable marker" it is unclear how the mere presence of the label which was knowingly added to the fluid would indicate the presence of the double-stranded moieties.

F1) Claim 10 is indefinite because "single-strand specific nuclease" lacks proper antecedent basis. Claim 1 has been amended to recite single strand oligonucleotide-specific nuclease. The claim is no longer directed to "single-stranded specific nuclease". Thus, "single-strand specific nuclease" lacks proper antecedent basis.

Conclusion

7. **No claims allowable.**

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Goldberg
February 26, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600